



Case review

Adverse event analysis in fatal cases of influenza A (H1N1) – A lesson from Poland



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ABSTRACT

During pandemic of influenza A (H1N1) in 2009 the relationship between mortality and medical errors, especially delayed antiviral treatment initiation, was highlighted in many studies. Our study was based on 5 fatal cases of pandemic influenza A (H1N1) hospitalized in Poland between November 2009 and February 2011. The material included data from medical documentation as well as testimonies from medical personnel and patients' families recorded during on-going lawsuits alleging medical malpractice. The risk factors of adverse events were: lack of typical symptoms, lack of detailed medical history, clinical masking of a "trivial" illness, doctors' ignorance and insufficient knowledge, several physicians treating the same patient during hospitalization. Recommendations for improving management of pandemic infectious disease include: an effective, quick and detailed system of information about the epidemiological threat, clear indication of units with diagnostic and medical possibilities, rational health policy and national system of closed claims and adverse event analysis.

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1. Introduction

2009 saw the start of an influenza pandemic due to an outbreak of a new A (H1N1) virus.¹ Even though the mortality rate was similar to that caused by seasonal influenza, the ease with which the new virus spread, its incidence and its clinical course suggested a certain specificity.² The first case of influenza A (H1N1) in Poland was diagnosed on 6th May 2009 – one month after the first case had been confirmed in Europe (in Spain).³ The greatest incidence was recorded in November and December 2009. However, 182 fatal cases of the A (H1N1) virus were confirmed between the start of the pandemic and 31st July 2010.⁴ According to an ECDC report, the total number of deaths compared to other European countries was high (sixth position), but the mortality rate was low (population rate < 0.5 per 10⁵). The highest number of cases of influenza A (H1N1) were reported in the United Kingdom, France and Spain. The highest population rate was in Estonia and Latvia.⁵

In order to determine the decisive factors in the disease's adverse course, a constructive evaluation of mistakes made by medical personnel, as well as any organisational issues or faults in the healthcare system is required.⁶ Such analysis allows for the

causes of adverse events to be evaluated; in this case, the fatal course of the A (H1N1) virus. This type of analysis is also important for preparing treatment regimens and indicating the adverse events in which errors may occur.^{7,8} The risk factors selected in our study may, by convention, be classified as "red alerts." Their rapid detection and elimination allows clinicians to provide a faster and more accurate diagnosis and to prescribe a suitable treatment regimen, which can also affect prognosis.

The situation in Poland during the pandemic influenza A (H1N1) was specific. The organisation of basic healthcare – poor availability of 24/7 ambulatory care, excessive selectivity of hospital admissions via A&E, only a small number of isolation wards, and an on-going conflict between healthcare providers and the funding institution (*National Health Service*) were just a few of the issues at play. In addition, the policy adapted by the Polish Ministry of Health was specific. Poland was one of the few EU countries that did not organise national pandemic influenza vaccinations and did not establish any vaccination recommendations.⁹

Therefore, any conclusions drawn by the authors of the study may serve as a warning to help solve pandemic-related issues in other countries, as the saying goes: "learn from the mistakes of others".

2. Materials and methods

A retrospective study of 5 fatal cases of influenza A (H1N1) admitted to different Polish hospitals between November 2009 and

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February 2011. All cases were confirmed for the pandemic influenza A (H1N1) virus by RT-PCR from nasopharyngeal swabs. The material included data from medical documentation (patients' full medical histories, medical reports, nursing documentation) as well as testimonies from medical personnel and patients' families recorded during on-going lawsuits alleging medical malpractice. The study protocol included the following information: age, gender, co-morbid conditions, type and evolution of clinical symptoms, course of the disease, number of medical appointments before hospitalisation, quality of medical history, decisive factors in the choice of medical-diagnostic strategy (test results, evaluation of medical data, efficacy of the treatment used, level of knowledge, possibilities of the healthcare system).

3. Results

In the 5 fatal cases of influenza A (H1N1) in 2009 analysed, the patients' ages ranged from 23 to 32 [Table 1] and 2 males and 3 females were included. 3 patients (women) had underlying conditions – severe disease risk factors: unidentified arthritis treated with methylprednisolone, pregnancy and obesity. None of the patients had been vaccinated for the seasonal and pandemic (H1N1) influenza virus. 3 patients had contact with people with flu-like symptoms (H1N1 not confirmed). All the patients had typical flu-like symptoms: fever, cough and fatigue. The duration of symptoms before the first consultation with a doctor ranged from 1 to 4 days.

In 4/5 cases, the first contact was with a family or emergency physician. In 1 case a pregnant patient presented directly at the hospital. In all cases, during the first contact with the physician, there was no suspicion of pandemic influenza despite the fact that the symptoms presented, epidemiological situation and data in the patient's medical history pointed to this. A non-specific viral infection, pharyngitis or tracheitis, was diagnosed instead. In one case, non-specific flu was also diagnosed. However, an antibiotic was administered to 4/5 patients before their hospitalisation. A test wasn't performed during the first medical intervention in any of the influenza A (H1N1) cases. 4 patients had consulted a total of 13 physicians before being hospitalised. The number of appointments before the decision to hospitalise was made ranged from 0 to 5 in individual patients. The duration of symptoms before hospitalisation ranged from 6 to 8 days and in 4/5 cases, the decision to hospitalise was made by the patient's rapidly worsening general

condition or the onset or exacerbation of respiratory distress. During hospitalisation, an influenza test was performed immediately in 2 cases but in the other cases the test was performed with a delay of 2–4 days. Oseltamivir was administered 7–9 days after the onset of the illness. Only 1 patient's treatment began on the day they were admitted to hospital. The delay ranged from 1 to 4 days in the other patients.

The total number of physicians who treated the 5 patients – until the infection was diagnosed – was 32. Only 1 openly admitted to their lack of knowledge of the specific medical procedures during the influenza A (H1N1) pandemic. Among the 32 physicians: the cause of the wrong procedures being used was identified in 14 cases; 5 physicians claimed to notice no "typical" symptoms of pandemic flu (including no signs of respiratory failure, no presence of auscultatory changes and a lower temperature after antipyretics). All other physicians blamed the duration of the symptoms being too long or too short, the disease's mild course, negative screening test results, efficacy of antibiotic therapy in other sick relatives and consultations with other specialists (internists).

In all cases and at all stages of treatment, there was no detailed medical history, no comprehensive data available on the disease's development, current symptoms or their evolution. In 2 cases, despite suspected pandemic influenza, an incorrect diagnostic–therapeutic strategy involving delayed antiviral therapy was used while test results were pending. During intensive therapy, there was no or very little access to advanced treatment methods for patients with acute respiratory failure (ECMO, CO₂ elimination). Nitric oxide therapy (NO) and oscillatory ventilation were used in just 1 case.

4. Discussion

Detailed analysis of the causes of the treatment's failure suggests that, in all cases, the patient's death was due to a delay in determining a correct diagnosis and administering treatment. The prognosis may be improved by increasing the chances of a faster diagnosis and eliminating causes of delays.

The course of the pandemic influenza in its initial stages did not involve the occurrence of pathognomonic symptoms which would have made it easy to distinguish it from seasonal influenza or other respiratory infections. Despite the pandemic alert, physicians did not routinely diagnose patients with the A (H1N1) virus infection, but diagnosed other infections, which were more typical and likely in their opinion. The reason for this might have been that they were not aware of the epidemiological risk and they possessed insufficient knowledge.

Another factor contributing to the diagnostic error was a lack of details when taking the patient's history and lack of knowledge of the symptomatology of infectious diseases. Analysis of the documentation and testimonies obtained from patients and their relatives indicate a clear lack of detailed questions concerning epidemiological factors and the duration and evolution of symptoms in the histories collected. The treatment regimens involved "standard" solutions to an infection problem, i.e. diagnosis based on clinical symptoms and administration of an antibiotic "just in case." Such procedures, despite the lack of indication for antibiotic therapy, were applied in the majority of cases investigated.

Another risk factor was the patients' young age. Such a scenario – a young patient with symptoms of an upper respiratory tract infection and no chronic diseases – misled the physicians and lead them to predict a mild course of the illness. Meanwhile, the A H1N1 pandemic was characterised by an atypical and severe course of infection among young people (20–40-year-olds).^{2,10–12} With this in mind, despite intuition, the physicians should have clearly recognised "young age" as a warning sign for a potentially severe course of the disease.

Table 1

Patient data.

	Case 1	Case 2	Case 3	Case 4	Case 5
Gender	M	K	M	K	K
Age	29	31	32	23	29
First contact with a doctor – day	2	1	4	2	3
Number of doctors' visits before hospitalization	3	5	4	5	3 (by phone)
Hospital admission – day	6	8	7	7	3
Influenza suspicion – day	7	8	4	7	6
H1N1 confirmation	8	10	7	7	7
Start of antiviral therapy – day	7	9	8	7	7
Death – day	27	11	15	9	17
Severe disease risk factors	None	Obesity (BMI 40)	None	Chronic arthritis	Pregnancy 31 weeks
Contact with sick people	Unknown	4 family members	2 family members	Unknown	2 family members

A similar problem concerned the patients' initially good health, which did not require immediate action either. However, with this pandemic flu, the dynamics of the course of disease varied.^{2,10,13–17} In a short period of time it could lead to respiratory failure, which affected prognosis negatively. An appropriate strategy against pandemic influenza is to use a far more serious scenario than that which the initial clinical data may indicate. In the cases investigated, patients' initial good health was one of the reasons that led to decreased alertness and the delay in diagnosis and treatment.

Another seemingly insignificant risk factor was the large number of physicians diagnosing each case. This is mainly due to the organization of the healthcare system. Patients are cared for by the general practitioner during the day. At night and during public holidays healthcare is provided by a so-called overnight medical service or in the emergency rooms of hospitals – where doctors change every day. Through analysis of the medical history and collection of detailed anamnestic information, the doctor is able to determine how many physicians the patient has already consulted beforehand. A large number of specialists, just like in our study, is cause for alarm as it means that many people have consulted on a patient's issue and it remains unresolved. Such a situation also leads to a “blurred” feeling of responsibility for the patient.

In addition, the psychological factor played a vital role in the induction of adverse effects by influencing doctors' treatment procedures. Data included in the testimonies and interrogation protocols confirm doctors' disbelief in the possibility of influenza A H1N1 in individual patients. The threat seemed remote, unrealistic, even “imaginary” and this was partly due to the relatively low number of cases reported and decreased epidemiological alertness. A patient's excessive concern for their own health made some physicians step back from the problem. The escalation of the risk projected by the media lead to just the opposite – doctors' scepticism. Such observations confirm the results of previous surveys and studies illustrating such controversies.^{18,19} A practical solution to such an emotional attitude from professionals could include actions aiming to “tame” the threat by showing it and providing appropriate treatment regimens.

The medical-diagnostic strategy also “fell victim” to general scepticism. In the early diagnostic stages of the cases studied, no tests for pandemic flu were performed; explanations mentioned their poor availability and long waits for results. Another explanation given by physicians was that their attitude was appropriate due to the shared belief in the low efficacy of antiviral therapy. There were two reasons for this: the incorrect assumption that antiviral therapy can only be commenced after a positive test result is obtained and a lack of sufficient knowledge about how to interpret negative results. Due to the limited sensitivity and specificity of the screening test in particular, the negative result did not exclude the infection. In some cases, in response to allegations of delayed treatment, test results indicating the limited efficacy of antiviral therapy were used.^{20,21} It was also emphasized that the duration of the drug's action was weaker 48–72 h after the onset of symptoms. It was wrongly assumed that since the therapy did not produce positive results with advanced symptoms of infection, there was no need to administer it or perform diagnostic tests. The response to such a “dangerous” attitude is a diagnostic algorithm and its effect on therapeutic treatment. In the case of pandemic flu, the decision to begin antiviral therapy did not depend on obtaining the results of the preliminary virological test, which should have been emphasized when establishing the guidelines.^{22–25}

Mere knowledge of the pandemic is not enough for appropriate actions to be taken. Information about the pandemic was broadcast widely – mainly in the media. This could have lead to a subjective feeling of threat however, it did not prove sufficient enough to provoke effective medical procedures. Even though anxiety

surrounding the disease may trigger irrational actions ranging from panic to ignorance, such emotions should not apply to a medical professional.²⁶ For accuracy and optimal diagnosis time, the availability of specialist knowledge in the form of concrete information to determine the rules of action is essential. A lack of such information leads to errors in disease recognition; this is demonstrated in our study. Statements from the Polish Minister of Health were delivered with a noticeable delay compared to the guidelines given by the WHO and they were also much less precise.^{3,27} Even though the first official recommendations from the WHO regarding pandemic influenza procedures were announced in May 2009, the Polish Ministry of Health waited to deliver until 3rd August 2009 to issue a suitable statement.^{1,3} Subsequent Polish recommendations failed to provide clear instructions regarding diagnostics and therapy for pandemic influenza. It is also worth mentioning the trivialisation of the threat by Polish physicians, their ignorance of the recommendations, lack of trust in scientific sources of information and tendency towards authoritarian evaluation based on their “own beliefs”.¹⁹ The manner in which the statements were delivered was limited to sharing information with healthcare providers. No actions promoting suitable procedures were available. In situations like the above, the best results are obtained, not through official directives, but rather through marketing-like campaigns; these campaigns assume *a priori* that sceptics need to be convinced. Another good example of an ineffective information flow may be one of the cases investigated: a hospital where the diagnosis of pandemic influenza and start of treatment was delayed had its own intranet, through which all current directives and guidelines were distributed to physicians. Information about the pandemic flu procedures was handed out 16 times; however, it still did not improve the medical personnel's poor knowledge. It seems that, apart from the written directives, a good aid in the effective spreading of information would be mnemonics-based brochures and posters etc. conveying the necessary information through colours, images and charts and aimed at both physicians and patients.

It is also worth mentioning that none of the patients were vaccinated against seasonal (in Poland vaccinations against influenza are recommended but not reimbursed) and pandemic influenza. The pandemic vaccine, as a result of the policy adopted by the Polish Ministry of Health, was not available in Poland but it was possible to order it from other EU countries, including neighbouring countries. The reasons behind such procedures were based on cost-saving measures, although the results of tests and recommendations clearly indicate that the opposite strategy would have been more rational.^{28–31} “Economisation” was commonly accepted and used to prove a rational health policy. This situation added to the disrespectful attitude towards the threat of pandemic influenza by increasing the risk of adverse effects.

The manner in which Polish healthcare organisations were organised also had an indisputable effect on the adverse results of applied therapies; access to specialists was poor (small number of isolation wards) as was access to units where confirmatory diagnostic tests (PCR) for the A (H1N1) virus could be carried out. Although difficulty accessing specialist diagnostics is not an obstacle to the implementation of appropriate actions, it does affect the tendency to trivialise problems and avoid procedures that are not readily available. Such obstacles can be tackled by clearly defining the sources through which the physician in charge can receive specialist assistance.

The doctors, whom forensic experts have identified as responsible for the malpractice, have been prosecuted under article 160 of the Penal Code – “Whoever exposes human being to an immediate danger of loss of life or serious impairment of health...”. According to the Polish Penal Code the maximum penalty for this crime is 3 years imprisonment.³² The Court may also issue additional penalties, e.g.

prohibition of practicing medicine. Currently, all lawsuits are still pending. Professional liability proceedings are being carried out simultaneously by the medical council. The maximum penalty is loss of the right to practice medicine, however this is very rare. In Poland there are no national systems to analyse such adverse events to improve the patient safety and eliminate medical errors.

5. Conclusions

Risk factors of adverse events in pandemic influenza A (H1N1) with an adverse course include:

- lack of typical (pathognomonic) symptoms (many viral infections have the same symptoms) – diagnosis difficulty increases the threat,
- the young age and initial good health of patients – misleading camouflage of a “trivial” illness,
- lack of detailed medical history – “common cold” does not require insight,
- a patient’s excessive concern for their own health
- doctors’ insufficient knowledge and tendency to trivialise the problem – the threat of pandemic is remote and does not “apply” to us,
- several physicians treating one patient – despite their number the problem returns, i.e. it is serious.

Recommendations for improving management of pandemic infectious disease include:

- effective, quick and detailed system of information about the epidemiological threat
- promoting correct diagnostic and treatment procedures through application of mnemonics in addition to official announcements, discrediting “media intelligence”
- clear indication of units with diagnostic and medical possibilities, particularly when their number is insufficient,
- rational health policy in the country; no tolerance for ignorance or risk
- promoting prevention methods, as well as public education
- national system of closed claims (rulings) and adverse event analysis.

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Conflict of interest

None.

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